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Zebrafish (*Danio rerio*) as a Model System for Diseases in Biological Studies

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MS and SS Contributed equally to prepared the original draft. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Background: Zebrafish (*Danio rerio*) are now a prime model organism in biomedical research due to their genetic similarity to humans, optical transparency in early development stages, and ability to be genetically manipulated with ease. With the prohibition of animal dissection after 2014, and the stringent ethical requirements for the use of rodents such as mice and rats, zebrafish offer a convenient alternative model for disease studies. Their small size, rapid embryonic development, and capacity for recapitulating human disease phenotypes make them particularly suited for the study of multifaceted diseases, like cancer, neurodegenerative diseases, and cardiovascular disease as compared to other model organisms.

Aims: The following review aims to investigate the growing value of zebrafish as a model organism in disease research and highlight improvements in cell imaging technologies that further enhance

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their merit. It also highlights their potential to replace traditional mammalian models in future biomedical research because of ethical, logistical, and experimental advantages.

Materials and Methods: The findings of previous scientific research studies and research articles that employed zebrafish as a model system in disease-related research have been gathered and summarized. A literature review was conducted to denote the way that zebrafish have been employed together with advanced imaging techniques to explore a variety of human diseases.

Results: Evolution of cell imaging technology has made high-resolution visualization of complex cell and molecular functions possible in zebrafish. It has been demonstrated through research that zebrafish model well most forms of human disorders, and one can achieve experiment outcomes within a short time frame as they grow rapidly. In addition, use of zebrafish circumvents some of the ethical challenges posed by traditional rodent models.

Conclusion: The combination of zebrafish as a model organism and high-class cell imaging technologies presents an unprecedented platform for therapeutic design, drug discovery, and disease modelling. With their many advantages and fewer ethical constraints, the zebrafish are poised to become a major model system in future biomedical and translational research.

Keywords: Zebrafish; model organism; biomedical research; genetics; developmental biology; neuroscience; cell imaging.

1. INTRODUCTION

The zebrafish. Danio rerio, is tiny а freshwater teleost that has gained tremendous prominence as an ideal model biological research. organism for use in It has been extremely useful for the analysis of developmental biology, genetics, and several mechanisms of diseases (Ma & Huang, 2025). Found in the freshwater rivers of South Asia originally, the species has flourished in the laboratory environment very well and has proven to be a very convenient organism for scientists to study (Stovek et al., 2024). Perhaps one of the most important qualities that make it so commonly used is its high rate of embryonic development, which enables researchers to witness significant developmental processes in a matter of a short duration. In addition, zebrafish embryos are clear, making it possible to directly observe change since land molecules are at various stages of development (Arunachalam et al., 2013; Hagio et al., 2023). Moreover, the organism permits high-throughput screening methods. which allow easy large-scale genetic pharmacological and studies (Menke et al., 2011; Sadamitsu et al., 2024). Owing to such exclusive features, zebrafish emerged as have now an invaluable resource for scientists seeking to comprehend human diseases at the molecular level and investigate possible therapeutic strategies with greater accuracy and efficacy (Maddula & Juluru, 2016).

2. ADVANTAGES OF ZEBRAFISH IN RESEARCH

2.1 Transparent Embryos and Development

One of the most unique features of zebrafish (Danio rerio) is their method of external fertilization and development, which differentiates them from a large number of model organisms. In contrast to species that are internally fertilized, zebrafish deposit their eggs in the external environment, making it simpler to observe and manipulate embryonic processes (Rama Krishna 2024). One especially beneficial et al.. characteristic of larvae zebrafish is their innate transparency, which grants scientists the opportunity to visually examine embryonic development and physiological processes in real time. This transparency renders invasive since methods unnecessary non-invasive imaging technologies can be used to observe developmental progressions at cellular and tissue levels. As a consequence, researchers observe can cellular migration, organ development, and structural differentiation during different development stages (Habenicht, 1860). Moreover, this aspect significantly eases the study of developmental pathways, making it possible for researchers to track molecular interactions and gene expression patterns with high accuracy. In addition, the zebrafish system has been essential in studying how organismal growth is affected by genetic mutations and has thus allowed for a deeper insight into congenital abnormalities and hereditary illnesses (Burggren & Bagatto, 2020).

2.2 Genetic Manipulation

Zebrafish (Danio rerio) are very amenable to a variety of genetic manipulation methods and are thus a versatile model organism for the analysis of gene function and disease mechanisms. Some of the most frequently used methods include gene knockdown strategies involving morpholino oligonucleotides, which transiently suppress gene expression to determine the function of individual genes during early development (Lin et al., 2022). Moreover, the CRISPR/Cas9 genome editing technology has transformed zebrafish research by allowing specific and heritable genome modification, enabling targeted gene knock-outs and knock-ins. Also, transgenic methods have dramatically increased the scale of zebrafish studies by enabling the introduction of extraneous genetic material to explore gene regulation and protein function in-vivo (Zhangji et al., 2023). These sophisticated approaches as a whole offer scientists strong tools to analyze the contribution of single genes, examine intricate genetic interactions, and create models that closely reflect human diseases linked to genetic mutations (Dorner et al., 2024). The capacity to produce stable transgenic zebrafish lines expressing fluorescent proteins has also increased the usefulness of this organism. This aspect enables real-time visualization of gene expression patterns, protein subcellular localization, and dynamic cellular behavior during development. As a result, zebrafish have emerged as a critical system for revealing basic processes and furthering biological our knowledge of genetic diseases (Bertho et al., 2021).

2.3 High Throughput Screening

Because of their relatively compact size, simplicity of maintenance, and short reproductive cycle, zebrafish (Danio rerio) have become a model organism of choice for high throughput screening of chemical and genetic modifiers. Their capacity to generate high numbers of offspring in a short time frame enables Scientists perform large-scale experiments to with statistically relevant sample sizes, making them highly suitable for drug discovery programs (Song et al., 2024). The effectiveness of screening using zebrafish has played a key role in the identification of potential therapeutic compounds for many human diseases, including

cancer. cardiovascular diseases. and neurodegenerative disorders like Alzheimer's and Parkinson's disease. In addition, their transparent embrvos allow for real-time evaluation of drug action at the cellular and molecular levels, yielding important information on mechanisms of action, toxicity, and off-target effects (Parng et al., 2002). The capacity to perform large-scale screenings within a relatively short period not only speeds up the discovery of potential drug candidates but also lowers the overall costs and ethical issues related to conventional mammalian models. Consequently, zebrafish has emerged as a strong and universally accepted system for promoting preclinical drug discovery and enhancing the knowledge of disease pathophysiology (ZeClinics, 2024).

2.4 Physiological and Genetic Similarity to Humans

Zebrafish (Danio rerio) have been found to display a high level of genetic similarity with humans, with research establishing that about 70% of human genes exist with an analogous zebrafish ortholog. Such a high level of genetic homology has made the zebrafish a critical model for researching human biology and disease. Specifically, key biological processes controlling essential functions like organogenesis, immune regulation, and metabolic processes are highly conserved in zebrafish and humans (Howe et al., 2013). These common pathways allow researchers to investigate developmental and physiological processes in a living system that very closely resembles human biology at the molecular and Currie. cellular levels (Lieschke& 2007). Additionally, the preservation of genetic networks provides researchers with an opportunity to examine the underlying origins of several genetic diseases. giving insights into disease progression that plagues human beings. By usina zebrafish models. researchers can determine the effect of certain mutations, study gene-environment interactions, and measure the effectiveness and safety of prospective therapy interventions (Zon & Peterson, 2005). The capacity to perform such studies in a organism possessing vertebrate similar physiological mechanisms increases the translational value of zebrafish studies, rendering it an irreplaceable tool in biomedical and pharmaceutical research directed toward enhancing human health outcomes (Santoriello & Zon, 2012).

2.5 Applications in Disease Modeling

Zebrafish (Danio rerio) have also been widely used as a model organism to study a wide variety of human diseases, reflecting their utility and applicability in biomedical research. They have been used effectively to explore the molecular and genetic mechanisms of different diseases, such as cancer, cardiovascular disorders, neurological diseases, and infectious diseases (Dooley & Zon, 2000). The capacity to model cancer in zebrafish has given researchers insights into tumor initiation, metastasis, and the impact of potential anti-cancer drugs. In the same manner, cardiovascular diseases have used the transparency of zebrafish embryos to study heart development, blood flow patterns, and the impact of genetic mutations responsible for congenital heart disease (Kalueff et al., 2014). In addition, zebrafish models of neurological including epilepsy, Alzheimer's diseases. disease, and Parkinson's disease, have aided the investigation of neural circuitry function, neurodegeneration. and the testina of neuroprotective agents. Furthermore, because they have a conserved immune system, zebrafish are a good model for infectious disease, allowing researchers to study hostpathogen interactions and test new antimicrobial therapies (MacRae & Peterson, 2015). All of applications highlight the extensive these versatility of zebrafish as a model organism, such that they constitute an invaluable instrument for tackling difficult biological questions and improving our understanding of human illness and health (Bowley et al., 2022).

2.6 Cancer Model Systems

Zebrafish (Danio rerio) have proved to be a successful model for research on a broad spectrum of cancer forms, such as but not limited to melanoma, breast cancer, and blood malignancies. Their usefulness in cancer studies originates from several central benefits, such as their transparency to light early in their life cycle, by which direct visual observation of the formation of tumors, tumor development, and tumor metastasis occurs within a live organism (Gut et al., 2017). This characteristic trait allows scientists to monitor, in real-time, cancer cell and microenvironment interactions and observe dynamic processes, gaining mechanistic insights cellular and molecular tumorigenesis into (Stoletov & Klemke, 2008). Zebrafish models have also made it possible to analyze genetic contributions to tumorigenesis and identify oncogenes, tumor suppressor genes, and

sianalina pathwavs that plav part in tumorigenesis. The capacity to transduce fluorescent probes into zebrafish tumor models further improves imaging methodologies, with the capability for precise monitoring of cancer cell angiogenesis, metastatic behavior. and progression. Additionally, zebrafish provide a high-throughput platform for drug screening that is effective, such that researchers can quickly test the efficacy and possible toxicity of new therapeutic agents in vivo. Consequently, zebrafish have emerged as a valuable asset in cancer research, filling the gap between mammalian models and in vitro research. eventually leading to the design of more effective cancer therapies and personalized medicine strategies (Patton et al., 2010).

2.7 Cardiovascular Research

Zebrafish (Danio rerio) have also been an exceptionally useful model organism for cardiovascular disease research, and they provide huge benefits for analyzing developmental and disease processes of cardiac function. Their comparative simplicity but extensive conservation of the cardiac structure allow precise analysis of essential processes including cardiac development, morphogenesis, and physiological performance. The optical clarity of zebrafish embryos also makes it possible to visualize in real-time heart allowing development. scientists track to heartbeat dynamics, patterns of blood flow, and vascular formation without surgical intervention (Feitsma & Cuppen, 2008). Moreover, the zebrafish heart develops very quickly and starts beating around 24 hours post-fertilization, allowing researchers to analyze early cardiac morphogenesis and congenital defects. Researchers have been able to successfully model several types of congenital heart defects using zebrafish, allowing them to study the genetic and molecular mechanisms that lead to structural and functional abnormalities in the heart (White et al., 2008). In addition, zebrafish have been used to examine the impact of genetic mutations on cardiac function, yielding useful information regarding the pathophysiology of arrhythmias, cardiomyopathies, and heart failure. The capacity to perform large-scale genetic and pharmacological screens in zebrafish further augments their utility in the identification of potential therapeutic targets for cardiovascular disease, thus making them a critical tool in the progress of cardiovascular research and drug discovery (Bakkers, 2011).

2.8 Neurological Disorders

Within the context of neurologic disease, zebrafish (*Danio rerio*) has been an important model for the study of a vast array of neurodegenerative and neuro-developmental disorders such as Alzheimer's disease, Parkinson's disease, and autism spectrum disorders (Saleem & Kannan, 2018). Their highly described nervous system and high level of genetic and physiological homology with humans make them great resources for the examination of brain function and disease pathogenesis (Karra & Poss, 2017).

Zebrafish also have an impressive neurogenesis ability, allowing researchers to investigate the processes involved in neuronal regeneration and genetic degeneration. Usina engineering methods like CRISPR/Cas9 and transgenic modeling, scientists have been able to model major aspects of human neurological disorders and conduct research on disease progression at the molecular and cellular levels (Saleem & Kannan, 2018). Environmental causes of the diseases, including exposure to a toxic diet, can also be studied in the zebrafish model in vivo, providing an integrated approach to the understanding of gene-environment interactions. In addition, zebrafish offer a cost-effective model for high-throughput drug screening, which the discovery speeds up of potential neuroprotective and disease-modifying drugs. The utility of zebrafish in neurological studies continues to grow, providing promising directions for unraveling the intricacies of brain disorders and developing therapeutic approaches (Newman et al., 2014).

2.9 Infectious Diseases

Zebrafish (Danio rerio) are being used with greater frequency as a versatile model organism in the study of infectious diseases, including host-pathogen interactions and immune responses. With their evolutionary close relationship to mammals and the presence of a functional innate and adaptive immune system, they are best suited to unravel the mechanisms involved in infectious disease (Schmidt et al., 2013). One of the greatest benefits of employing zebrafish within this discipline lies in the transparent nature of their embryos, meaning that scientists can watch immune responses immediately after exposure to a range of pathogens, from bacteria and viruses to parasites (Sullivan & Kim, 2008).

Undergo invasive techniques. Furthermore, zebrafish models have been used to investigate the genetic and molecular mechanisms of infection susceptibility and immune regulation, shedding light on the host's defense responses. Using genetic manipulation strategies, scientists generate transgenic zebrafish lines can expressing fluorescently tagged immune cells, which further improves the capability to monitor immune dynamics during disease development (Meijer & Spaink, 2011). In addition, zebrafish provide a high-throughput system for the screening of candidate antimicrobial drugs and the testing of new therapeutic approaches, substantially speeding up the process of drug discovery. Increasing applications of zebrafish in infectious disease research continue to advance the understanding of infection mechanisms, leading the way toward more effective treatments and prevention strategies against a broad array of human pathogens (Sullivan et al., 2017).

3. CONCLUSION

The zebrafish (Danio rerio) is an incredibly powerful and versatile model organism across a vast range of biological research, providing valuable insights into basic developmental mechanisms and disease mechanisms. Its many such strengths. as quick embryonic development, genetic tractability, and a large amount of physiological relevance to humans, render it the best fit for scientists interested in investigating the complexity of human biology and disease. With the capability to screen genetic and pharmacological compounds in large numbers and the clarity of zebrafish embryos, there is a live visualization of molecular and cellular interaction in real-time, greatly expanding research into both normal physiology as well as the pathogenesis of the disease. The zebrafish models also played a central role in promoting an understanding of several medical ailments, from cardiovascular cancer and conditions to neurological as well as infectious diseases. With growing advances in genomic engineering, imaging technologies, and computational biology, the field of zebrafish research promises to grow in scope even larger, offering human health and disease an even clearer window into secrets. As ongoing improvements in tools like CRISPR/Cas9 genome editing and the development of increasingly nuanced transgenic models continue, it is likely zebrafish will continue leading the way for biomedical research. Their continued use in disease modeling, drug discovery, and therapeutic development reinforces their value to the field of precision medicine and translational research.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative Al technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Sengupta et al.; Uttar Pradesh J. Zool., vol. 46, no. 10, pp. 94-101, 2025; Article no.UPJOZ.4886

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